BRITISH JOURNAL OF
TUBERCULOSIS
AND DISEASES OF THE CHEST

Vol. XL. July, 1946 No. 3

GENERAL ARTICLES

THE RELATIONSHIP BETWEEN PRIMARY AND ADULT TUBERCULOSIS*

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In spite of the fact that the connection between primary tuberculous infection and destructive pulmonary tuberculosis has been one of the central questions of debate in the study of the disease during the last twenty years, there are still widely divergent views about it. This is partly the result of variations in the epidemiological picture from country to country, mainly in the infection curve, but also in morbidity and mortality. An equally important cause of the diversity of views, however, is perhaps that these conditions have undergone marked changes in a relatively short period, and many writers have had difficulty in ridding themselves of the old familiar concepts. A quotation from Ibsen's play, " The Pillars of Society," is applicable here: " Truth is no long-lived Methuselah; an ordinary, well-founded truth lives twenty, at most thirty years." Many of the dogmatic statements concerning tuberculosis from the first decade of this century are no longer acceptable. We must abandon them.

I propose to consider *primary tuberculous infection* first. When the Tuberculosis Conference at Lisbon in 1937 agreed that infection now occurred chiefly during puberty and early adult years, the dogma of universal childhood infection received its death blow. The infection curve shows a somewhat different course in different countries, as well as within these countries according to density of population, the amount of existing infection and the effect of prophylactic work. But in most places the greatest amount of tuberculous infection now appears to occur after school age. Primary infection in the age group between 30-40 is not rare, and it is possible even between the ages 40-50. Although in larger cities 90-100 per cent. of the population is infected, in rural areas there is a certain number of individuals escaping infection. I do not consider it necessary to show curves or give percentages to amplify this.

* Read at the Annual Meeting of the Tuberculosis Association at Oxford, July 1946, in opening a discussion on this subject.

We are agreed upon the point that a large number of primary infections occur during adult life, a fact which is in no way changed by the difference of opinion concerning the details of tuberculin testing technique.

In the last few years we have become familiar with the *clinical-radiological picture* of primary tuberculosis. When conditions for observation are particularly satisfactory, we find that approximately one-third, occasionally one-half, of the primary infections are accompanied by demonstrable disease symptoms. The most important is the radiological picture with its characteristic hilar adenitis, the relatively extensive infiltration of the lung, often perihilar, the serous pleurisy and the hæmatogenous dissemination. The frequent occurrence of tubercle bacilli in the gastric content is also of great importance.

We are all well acquainted with the clinical manifestations of primary tuberculosis, which occupies a large place in the tuberculosis specialist's daily practice. We see them in children, adolescents and adults. One can hardly say that there is agreement on the question of the difference in the immediate reaction of adults and children to the primary infection. Hæmatogenous dissemination and miliary tuberculosis seem to be more frequent in children than adults. Hilar adenitis and perihilar infiltration are perhaps also less marked in adults. However, the difference is slight and hardly of any great importance.

Finally, we know that the *prognosis* in primary infection often is good. This is true particularly in " silent " infections, but primary clinical tuberculosis also has a favourable course in many cases. I shall return later to the fact that the disease may also be malignant and that the prognosis is less favourable for adults than for children.

In discussing *destructive pulmonary tuberculosis*, characterised by cavity formation, progression and the presence of tubercle bacilli in the sputum, and which without treatment usually leads to death, there is reason to stress the fact that this disease occurs very rarely in childhood. Both morbidity and mortality curves have had a characteristic maximum between the ages of 15 and 30 in most places for a number of years; but this age maximum now appears to have a tendency to level off into a more even distribution of cases throughout the adult years.

Because we formerly, perhaps with a certain right, assumed that primary infection occurred chiefly in childhood while destructive pulmonary tuberculosis was rare during that period, some authorities considered a " childhood type " and an " adult type " of pulmonary tuberculosis as opposites. To-day there is no foundation for such a division, and it merely contributes to a confusion of the concepts.

According to the Norwegian view, it is also unfortunate to distinguish between the " first infection type " and the " reinfection type " of pulmonary tuberculosis. It is important in dealing with these complex questions to have our terminology clear. Reinfection in general pathology means a new infection in a host in whom the original infection is completely extinguished, biologically healed; and the term should be used thus in regard to tuberculosis as it is used in syphilis. We may probably assume that such reinfection can occur in tuberculosis, but so rarely that it plays no practical rôle.

The correct designation for a new infection in an organism where the old

infection is still living is *superinfection.* I shall return later to the fact that superinfection probably plays a very small part, if any, in human tuberculous disease.

Tuberculous disease which does not develop in direct connection with a primary infection may be considered to have originated either from *reactivation* of latent foci or from *metastases* from foci in the lymph glands or other organs. In conducting a factual discussion of these conditions it is a distinct advantage to exclude the theories concerning allergy as far as possible. Ranke's theory of the immunological stages of tuberculosis has been most unfortunate in that it has clouded these issues. For the time being I believe that it is best to include all tuberculosis which does not develop directly from the primary process under the heading *post-primary.*

The relationship between primary infection and destructive pulmonary tuberculosis has three phases which we can discuss separately up to a certain point. In the first place, how long is the time interval between infection and the onset of disease or final death? Secondly, what pathogenic relation is there between the disease processes accompanying the primary infection and the fatal disease processes? Finally, what factors govern the course of the disease; what factors determine the individual tuberculous history?

The time interval is the question upon which we have reached the most general agreement. A wealth of clinical and statistical material is now available to show that the interval in most cases is quite short—under five years, often only from one to two years. The widespread use of dependable tuberculin testing, which may be said to have been reached, at least in Scandinavia, adds steadily to this total of cases with a short interval between infection and destructive pulmonary tuberculosis. In the Scandinavian countries we feel justified, with certain reservations, in using erythema nodosum as the basis for determining the time of the infection. One series of 300 patients with erythema nodosum followed for periods of up to sixteen years is typical. The cases were chiefly destructive pulmonary tuberculosis with a few of meningitis and bone and joint tuberculosis. The morbidity curve showed a high peak in the first five years after infection, particularly in the first year. The deaths were distributed over the first five years. In particular, Wallgren's figures showed that pleurisy most often appears within the first six months after tuberculous infection. If we investigate the interval between the pleurisy and later pulmonary tuberculosis more closely, as Scheel, among others, has done, we find that there is a large concentration of tuberculous disease in the years immediately following the pleurisy. The period after the primary infection appears in most cases to be short.

Scheel has also used another method to clarify the time interval, the use of statistics. Scheel pointed out the remarkable relative similarity of the curves for tuberculous infection (*i.e.*, tuberculin positive reaction), tuberculosis morbidity and tuberculosis mortality in Oslo in the 1920's. We may obtain a picture of new infections in the various age groups by plotting as a curve the increase in positive reactors from age group to age group, as Scheel has done for Heimbeck's investigations in Oslo. The curve begins to rise at 10 to 15 years, but its sharpest rise is in the next five-year period. The curve for cases of pulmonary tuberculosis notified in Oslo shows that in the case of

women this begins to rise sharply in the 10 to 15 years age group and reaches its maximum during the period from 20 to 30 years. The mortality curve rises parallel with that for morbidity, but it falls less steeply, corresponding to the long-drawn-out course of the disease. The steep rise in morbidity and mortality coincides with the age at which the number of new infections is greatest and the five-year period directly following. Scheel pointed to these features as further evidence of the close time-relation between infection, disease and death.

E. Dahl and J. Backer also showed the increase in tuberculin positive reactors from age group to age group in Oslo, 1943, as compared with Heimbeck's figures from 1929. Both the infection curve and the increase curve are advanced so that the maximum of new infections is now found between the ages of 25 and 30 years. As a parallel the maximum morbidity has also advanced five years during the same period.

Thus there are good grounds for the assumption that the time interval between primary infection and destructive pulmonary tuberculosis under present conditions is quite short for most cases, a fact which finds constant support from clinical observations. This does not preclude a number of individuals from appearing with the disease after a period of latency, even ten years or more. Accurate figures on the ratio between early and late cases cannot yet be given; but it seems evident that late cases are of minor practical importance.

For many years attempts to clarify the question of the time interval between infection and the disease have been based on observations of groups of tuberculin negative and tuberculin positive individuals over a given period of time with comparison of the morbidity in the two groups. Many such investigations have been published. Their results have been controversial, and the waves of controversy have waxed high. Actually, the over-simplified question, which is more dangerous, to be tuberculin positive or tuberculin negative? leads to no useful result. Höyer-Dahl long ago pointed out the great statistical sources of error in such a comparison. The main point is that in a group originally tuberculin negative, tuberculous disease can only occur in those who become infected with tuberculosis during the period of observation. Therefore, in order to determine the true morbidity in the negative group, we must determine the total number in that group who have become infected, an elementary circumstance which most investigators have overlooked. Other circumstances make such comparisons poorly adapted for clarifying the question of time interval between infection and disease. Heimbeck's well-known study of nurses is an exception in that all of the negative reactors became positive in the course of three years. The criticism directed at Heimbeck's investigations, that some of the cases were typical primary processes, is partly justified; but we must also note that both the pulmonary tuberculosis and the deaths in Heimbeck's material occurred largely in the negative group.

If we can say that there is some agreement on the concept that the time interval between infection and disease is in many cases quite short, we must admit that there is a wide diversity of opinion on the question of the pathogenitic connection between the manifestations of the primary infection and those of destructive pulmonary tuberculosis. A very short interval, a few

months or even weeks, does not in itself mean that a destructive process started in the area of primary infection; a new focus in another part of the lung can develop in a very short time.

Theoretically we have two leading possible causes of the development of destructive pulmonary tuberculosis: it can develop *directly from the primary focus* or the immediately surrounding tissue by breakdown, or it can start from *a new focus* in another part of the lung.

If we disregard Norway, we find that the hypothesis of origin from a new focus has had a general and widespread following. The discussion has chiefly been concerned with the mode of origin of the new focus: whether it arises from a superinfection from outside, from a hæmatogenous spread or as a result of so-called " lymphoglandular endogenous reinfection." There has also been disagreement as to whether the causative metastatic processes occur early in the primary infection period or are a later development. A great deal of the discussion has centred around the most common site of the new focus and its radiographical appearance.

Pathological anatomy contributes only to a limited extent to the solution of these problems because the marked changes in fatal tuberculosis prevent an accurate reconstruction of the course of the disease. Many sins have been committed in this field. We do best to limit ourselves to the clinical and radiographic investigations.

We did not reach reasonably firm ground in this question until the end of the 1920's, when Assman, Redeker, Simon and others published their radiographic investigations showing the relatively acute beginning of pulmonary tuberculosis with limited infiltrations, usually below the clavicles. Similar observations were also made simultaneously in France and the U.S.A. The old teaching that the disease had a stealthy apico-caudal development from tiny apical foci appeared to have received a mortal blow.

The new and valuable impulses introduced by Redeker and other German investigators were their careful radiographic series examinations and the demonstration of isolated infiltrations which by their breakdown form the origin of a rapid development of pulmonary tuberculosis. However, there was one basic error in these investigations: they ignored the tuberculin reaction. This was all the more serious because the new German teaching was centred on the allergic condition. Redeker, who was a firm apostle of the old belief in universal childhood infection, claimed without any basis of tuberculin examinations that the Frühinfiltrats were new infiltrations in previously infected individuals and that superinfection played an important part in their development. Actually, there were many circumstances which could favour an interpretation of Frühinfiltrat as representing the primary infection: the radiological appearance of the infiltration which could not be distinguished from the primary focus; localisation entirely similar to that of the primary infection; frequently coincident hilar adenitis, absence of calcification in the glands, and, finally, the circumstance that the patient had been exposed to infectious tuberculosis a short time before. Furthermore, the Frühinfiltrat occurred in the age groups in which we now know that primary infection is most frequent.

Any examination of this kind in order to give us valuable information con-

cerning the relationship between primary infection and disease must commence at the time of the primary infection—that is, at the time when the tuberculin reaction changes from negative to positive. Therefore, neither Redeker's nor Brauening's later series can clarify our problem.

As early as 1928 Scheel and Heimbeck posed the question as to whether or not infiltration which immediately precedes a destructive pulmonary tuberculosis is actually a part of the primary process. They emphasised the necessity of examination of series of individuals with primary infections continued over a long period in order to solve this problem. In the following years a number of single cases were published in Norway (Giertsen, Harboe, Heimbeck, Frostad) which clearly demonstrated breakdown of the primary focus with following destructive pulmonary tuberculosis. The first larger study of this problem was presented by the Swedes Malmros and Hedvall in 1938. In systematic investigations of 3,336 students and probationary nurses they detected 133 cases of active tuberculosis. Forty-seven cases were found in individuals who at the beginning of the investigation reacted negatively to tuberculin. Malmros and Hedvall claim to have shown that pulmonary tuberculosis in the cases primarily infected in adult life commenced in general as small or rather large, often multiple, cloudy spots, located in the supraclavicular region or in the first intercostal space or in both places simultaneously, what they called " subprimary initial foci." The interval between primary infection and destructive tuberculosis was in many cases rather short. Fully typical Frühinfiltrats without mottling in the surrounding areas occurred very seldom in their material. Nor were they able to show a diffuse hæmatogenous dissemination in more than a few isolated cases. Direct development of destructive pulmonary tuberculosis from the primary infection zone was not found in any case by Malmros and Hedvall.

Malmros and Hedvall's study is not large. Only 19 of the 47 cases among the tuberculin negative had destructive pulmonary tuberculosis. However, their work was the first step along a thorny path, and demonstration of the " subprimary initial foci " is of great interest, even though this point will doubtless be the subject of much discussion. Demonstration of comparatively *small* foci as the origin of pulmonary tuberculosis is somewhat in opposition to the teaching of Redeker and others of a beginning with relatively *large* infiltrations. As Brauening has shown, this opposition is probably not actual but is the result of variations in the description of the radiological findings. The demonstration of supraclavicular foci as a possible starting point for destructive pulmonary tuberculosis by Malmros and Hedvall is of particular interest.

In 1944 Simon Frostad published a large study of primary infections which he had followed with frequent radiological examinations. This work was originally inspired by Scheel. From a basic material of about 500 primary infections Frostad chose 135 cases in which destructive pulmonary tuberculosis developed after a varying time interval. In 48 of these 135 cases Frostad claimed to have shown that destructive pulmonary tuberculosis developed directly from the primary focus or the immediately surrounding area by breakdown. Even though there may be some doubt in a few cases as to the foundation for this conclusion, the fact remains that in the great majority of the

cases Frostad has been able to demonstrate radiologically the presence of cavitation in the primary infection area. The destruction was demonstrated less than four months after the first clinical symptoms of primary tuberculosis in a total of 25 cases.

This is quite a sensational fact. It is true that we knew from the frequent occurrence of tubercle bacilli in the gastric fluid that there must be destruction in the lung tissue by primary infection; but the question takes a different position after radiological demonstration of cavitation.

In most of Frostad's cases the further development of the tuberculous process was arrested by pneumothorax treatment. Thus we do not know how malignant the demonstrated destruction would have become. However, in a number of cases these destructive primary infections progressed and showed a picture of malignant primary tuberculosis in spite of treatment.

In this work Frostad has presented strong support for Scheel and Heimbeck's hypothesis that destructive pulmonary tuberculosis develops in some cases from a direct breakdown in the primary infection area. It is too early to say whether it is the primary focus itself that breaks down or another focus developed in the early spread of the process to the immediately surrounding tissue. It is also possible that the majority of such primary cavities would show a tendency to spontaneous closure if left to themselves. Most of them are small, usually less than 30 mm. in diameter. We are familiar from Cold's work, among others, with the marked tendency to spontaneous healing of such small cavities.

By serial radiological examinations Frostad has further shown in 11 cases that the quiescent primary focus can be reactivated after a long interval, break down and give rise to destructive pulmonary tuberculosis. The interval between the primary phase and the reactivation may be several years. This manner of development must also be said to have a certain practical importance, as Tuxen has maintained for some time.

Frostad's material also included a number of examples of commencing destructive pulmonary tuberculosis from an entirely new infiltration at another site in the same lung or in the other lung. He found that these initial infiltrations were usually rather large at the time of their first discovery, usually more than 20 mm. in diameter as measured on the plate, and in appearance much more like a Frühinfiltrat than Malmros-Hedvall's subprimary initial foci.

For a more complete survey of these lesions we need a number of inclusive investigations of series of primary infections observed with frequent radiological examinations throughout a period of many years. At the present time we know that the radiological picture of incipient destructive pulmonary tuberculosis can be divided into at least four different types: first, the relatively large infiltrations of the Frühinfiltrat type which may be found anywhere in the lung, though seldom in the region above the clavicles; second, the multiple smaller infiltrations to which Malmros and Hedvall called attention, and which are usually located in the supraclavicular area and the first intercostal space; third, the small, spotty shadows seen covering a larger or smaller area of the lung and evidencing hæmatogenous spread of the disease; fourth, multiple soft foci which are apparently a special type of hæmatogenous dis-

semination. It seems very likely that the two latter types are of much less importance than the two first.

We also have at least four different possibilities in the pathogenetic problem: (1) Direct development from the primary lesion or its immediate surroundings; (2) reactivation of latent primary foci; (3) metastatic foci of either hæmatogenous, lymphogenous or bronchogenous origin; and (4) new foci caused by superinfection.

We do not attach any great significance to superinfection, as I have mentioned previously. There is hardly any doubt that superinfection does occur and that it has a certain importance in the maintenance of tuberculin sensitivity. However, we do not believe that superinfection has been shown to have any decisive bearing on the question of health or disease.

Thus it is the hereditary resistance, the living conditions, primarily nutritional and working conditions and, finally, age which are the decisive factors. As far as age is concerned, we know that destructive pulmonary tuberculosis occurs only rarely in childhood, but we know little more with certainty.

Summary

(1) The great majority of primary tuberculous infections now take place in the same age groups in which we find the largest percentage of destructive pulmonary tuberculosis.

(2) The time interval between the primary infection and the destructive pulmonary tuberculosis is in most cases less than five years, very often only one or two years.

(3) Primary tuberculosis is not always benign. Radiologically demonstrable breakdown is no rarity. In some cases primary tuberculosis is apparently very malignant.

(4) There is no doubt that destructive pulmonary tuberculosis begins in many cases with a new infiltration which must be assumed to have metastatic origin.

(5) The infective dose and superinfection have no effect on the prognosis of primary infection. Age, heredity and environment are the leading factors.

The most important practical consequences of this view are that demonstration of the primary infection by tuberculin tests is of decisive importance and that the infection must be carefully watched, particularly in the first few years after it has been contracted.

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THE RELATIONSHIP BETWEEN PRIMARY AND ADULT PULMONARY TUBERCULOSIS*

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The mortality graph of tuberculosis in this country is like a photograph of a long mountain range with two high peaks and an intervening plateau. The two peaks are those of childhood and young adult tuberculosis, whilst the low land between represents the disease in the later school years. But only a lack of stereoscopic vision would lead us to assume that this is all one mountain range. There are, in fact, two. In the foreground is a range representing childhood tuberculosis, which has its summit at the age of five and which reaches low ground towards the end of the school period. Behind this is another, reaching its highest point in young adult years but never reaching the plain again. To continue the analogy, these two ranges are different geological formations thrown up in different ages and we have to measure them from a distance with such surveying instruments as we possess.

Now let us drop the metaphor and ask ourselves whether as individuals we recapitulate in our own experience the community graph we have been considering. Obviously not, because this is a mortality curve. But does the morbidity experience of the individual follow similar lines? This is the question before us. Some 75-90 per cent. of the children of the large European cities before the first World War gave positive von Pirquet reactions by the end of the school-leaving age. There is some reason to believe, however, that the position has now changed, and more recent figures would suggest that infection of the younger generation is diminishing. In other words, the view held thirty years ago that those who dwelt in large cities almost invariably experienced their initial infection with the tubercle bacillus in childhood, and that most of the young adult tuberculosis was a recrudescence of childhood infection cannot now be maintained. Indeed, it would seem more reasonable to assume that we all receive our primary infection at different ages according to our individual adventures in community living, some of us in the home when quite young, others later in the outside world at a considerably older age.

Robert Koch laid the foundations of our study when he described what has ever since been called Koch's phenomenon. It is not necessary to quote the whole of this historic description. Here are salient points as modified by later researches.

1. If a normal guinea-pig is inoculated intracutaneously with a pure culture of tubercle bacilli the wound as a rule closes and in the first few days seemingly heals.

2. After ten to fourteen days, however, there appears a firm nodule which soon opens, forming an ulcer that persists until the animal dies.

3. Quite different is the result if a tuberculous guinea-pig is inoculated

* Read at the Annual Meeting of the Tuberculosis Association at Oxford, July 1946, in opening a discussion on this subject.

intracutaneously. [It is best to use animals that have been infected four to six weeks previously.]

4. In such an animal also the wound closes at first, but in this case no nodule is formed.

5. On the next or second day afterwards the area becomes indurated and assumes a dark colour.

6. These changes do not remain limited to the inoculation point but spread to involve an area 0·5-1·0 cm. in diameter.

7. In succeeding days the altered skin becomes necrotic.

8. Finally it sloughs, leaving a shallow ulcer which usually heals quickly and permanently.

9. After the first inoculation bacilli reach regional lymph nodes in one to four hours; after the second they take as long as four days.

10. This striking effect is produced not only by living tubercle bacilli, but also by dead bacilli.

Much water has gone under the bridges since Koch made this classic pronouncement. On the whole, however, the facts he noted have stood the test of time, though there have been criticisms and modifications. The most important are those relating to dosage and the time interval. If the dose of the primary infection be small, there may be no sloughing at the point of inoculation; if the re-infecting dose also be small, again there may be no slough. Much depends on the interval of time between the two doses. But the most significant part of the reaction is the necrosis. It is the cardinal sign of re-infection. This is brought out more clearly by histological studies. But it is important to notice that if the dose is sufficiently large necrosis and sloughing occur, too, in the primarily infected animal, because the disease in the guinea-pig is progressive, and progressive disease is its own sensitising agent. This point seems to call for emphasis all through our studies. It is a source of much perplexity, and perhaps we have been misled by too much emphasis on the guinea-pig. There is nothing more striking in the pathology of tuberculosis than the infinite variety of the reaction in the different animal species, and at the moment we cannot with any degree of certainty correlate these reactions. Rich, indeed, believes that there is really no correlation between the degree of hypersensitivity and that of acquired resistance. Moreover, Koch's phenomenon was worked out on the guinea-pig in an experimental infection with a known dose; and we always come back to the old question, Does it bear any relation to the haphazard infection in the human subject?

Here there appear to be two schools of thought. The one believes that man receives only one infecting dose of tubercle bacilli in his lifetime and that whatever else may befall him in the way of tuberculosis it will be a lesion arising from his own original infection which has never died out. In this case the principles of Koch's phenomenon, if they can be applied to man at all, need considerable modification. The other school assumes that the re-infecting dose is a fresh infection but says little or nothing about the fate of the original dose. In Koch's phenomenon in the highly susceptible guinea-pig we feel fairly certain what happened to the original dose; it went on multiplying rapidly to the end. In man this is not necessarily the case, and

here the analogy between the experimentally infected guinea-pig and man seems to me to break down. Many of our speculations about tuberculosis in man would be cleared up if we could ascertain the fate of the original dose of bacilli which he received.

Now let us turn to the evidence of the tuberculin test, and here I would refer you to D'Arcy Hart's admirable memorandum on the value of tuberculin tests in man. We are probably all agreed that tuberculin sensitivity implies infection. The difficulty is to determine whether, in D'Arcy Hart's words, " extinction of infection is followed by complete loss of skin reactivity to tuberculin." Most observers are not prepared to answer this question categorically. Almost all the earlier investigations were made with the von Pirquet test, whilst the later series have usually been tested with the Mantoux technique and the evidence is equivocal. The point that stands out most clearly is the decline in the percentage of positive reactors in the childhood groups since the original surveys were made before the first World War. At present we are learning a good deal about the young adult group in Mantoux negative nurses in tuberculosis institutions; we find, for instance, that there is a difference in the speed with which they become positive when they are exposed to the environment of one hospital and in the time relation between the appearance of the positive reaction and the initial illness if such occurs. The nature of this illness, too, is significant; it is commonly a pleural effusion and may be preceded by erythema nodosum. Unfortunately, we know very little about the initial illnesses of those nurses who arrive at hospital with Mantoux positive reactions. Indeed, as far as the population outside hospital is concerned, I think the time has come when intensive observations on a small series of cases over a long period are needed rather than more mass figures on single tuberculin tests. Just as we have come to regard the serial X-ray as essential so we may have to pay more attention to the serial Mantoux test than we have done in the past. To abandon it after the first positive as the end of a chapter in the patient's history which need not be reopened seems hardly satisfactory. The first few weeks after the appearance of a positive tuberculin reaction is a critical period in a patient's career about which we should like to know much more than we do, and serial X-ray films and sedimentation-rate tests are essential.

Our conception of the relation between the primary and adult forms of tuberculosis depends really, however, on our recognition and interpretation of the primary complex as seen in the radiogram. Thanks to the work of Ghon and his school in the post-mortem room, we are in the main nowadays agreed in our views about the primary focus as its starting point. It is true that these are individuals who have so little immunity, or alternatively in whom the infecting dose is so large, that this focus is obliterated in an extensive caseous lesion reaching the dimensions of fatal bilateral broncho-pneumonia or an acute disseminated tuberculosis, but such cases are fortunately rare. The next landmark is the post-primary stage. This is much more difficult to define and, after all, any event up to the end of the story must be post-primary. In the case of pulmonary disease it is best to confine the term, however, to those lesions which are found between the occurrence of the primary focus and the onset of bronchogenic spread. The most prominent of these is the initial

pleural effusion in the adolescent and young adult. The time sequence of the rest is not so clear. Perifocal satellite lesions around the focus spread to the lymphoid follicles in the walls of the small bronchi. The disease may become indolent or quiescent at this stage, or it may progress until a small caseous lesion ulcerates into a bronchus. This event, I would suggest, marks the end of the post-primary stage and the beginning of the chronic bronchogenic excavating lesion of the adult, the outward and visible sign of which is the appearance of sputum.

These are the lesions as we see them in those instances where the primary focus does not heal, but is this always the case? It seems not unlikely, too, that the anatomical and histological details of the primary complex vary in different countries according to the natural immunity of its people, especially its children. In this country the most intensive study is that of Blacklock. In a series of 1,800 consecutive autopsies made at the Royal Hospital for Sick Children, Glasgow, on children ranging from a few hours old up to thirteen years he found 283 with tuberculous lesions, of whom 173 (61·1 per cent.) had a primary lesion in the thorax; 101 (35·7 per cent.) in the abdomen and 6 (2·1 per cent.) in the cervical glands, whilst in 7 (2·5 per cent.) instances the primary lesion was not found.* In the first year of life naked-eye evidence of healing was found in only one case (1·7 per cent.). During the second year this percentage rose sharply to 34·9, and at the same time there were signs of encapsulation of cavities. The percentage rose again to 38·1 in the third year and after that the cases were too small in number to be statistically significant, but it was only in the fourth and fifth year that calcification of the primary lesion could be detected with the naked eye, and no completely fibrosed or calcified primary focus was found in the whole investigation. These findings are most striking and should be compared with those of Sir Harold Scott recorded in his memorandum on tuberculosis in man and the lower animals. The first part of this research was made on three hundred cases of fatal tuberculosis among Chinese of the labouring classes in Hong Kong, most of them children, and the second on a series of wild animals dying of tuberculosis while in captivity in the Zoological Gardens in London. In this series only one instance was noted amongst the children of an old fibroid or healed focus which occurred in the lungs of a child aged three. Although in the main the findings in this Hong Kong series correspond with those of European observers, there were features which merit emphasis, such as the absence of one-half of the primary complex—*i.e.*, either the lung focus or the gland—very early cavitation (the earliest in seven weeks) and the undue prevalence of meningeal blood spread.

On the whole, therefore, the evidence for the complete healing of the primary complex in childhood is not as conclusive as we should like it to be, but one point is clear: the older the child the more likely the lesion is to heal. Personally, I am more favourably impressed with the healing of abdominal than I am with pulmonary primaries, whilst cervical gland complexes are the most hopeful of all. Unfortunately, the pulmonary group is the largest. It may be significant in this connection to note in passing that, in the guinea-pig, infection by way of the intestinal tract is less certain and needs a larger dose of bacilli than does infection through the respiratory tract.

* There were four cases of double primaries.

In the adult we are faced with the difficulty of deciding upon the age of the primary focus. Is it a relic of a childhood infection or is it a true adult primary focus? It is more fibrotic and the hilum gland is a less prominent part of the picture than in the child, whilst blood dissemination is less frequent. Terplan has shown that first tuberculous infection may occur quite frequently after puberty. In the age groups 18-30 his percentage was 71, and this figure rose steadily to old age, when it became 97 after the age of 50.

He agrees with other observers that calcification of the primary tuberculous lesion may occur in less than a year. Puhl, indeed, believes that it may occur in even a shorter period—viz. 2-5 months in healthy individuals. Terplan deduces that the age factor does not necessarily alter the anatomical appearances of the primary focus, and that the view that increasing age brings with it less involvement of the lymph nodes draining the site of the primary infection needs modification, whilst he goes so far as to deny the statement of Myers that the appearance of the primary complex after the age of 20 is a myth. In the small series of autopsies on white adults in America he has also shown that the primary foci may be unaccompanied by infection of the regional lymph nodes even with carefully selected serial sectioning—a fact which Sir Harold Scott demonstrated in the Hong Kong children also.

But perhaps the most significant part of Terplan's work is that which deals with the question of re-infection. He has collected a series of post-mortem records in which the first tuberculous infection was represented by a completely calcified complex, whilst another complex of the secondary infection was also present. The two complexes were found in a different lung or in a different lobe, the one in a completely stony stage, the other in a caseous or calcareo-caseous but differing in no way from the typical primary complex. He has published two instances of a recent typical complex with true exogenous re-infection and hæmatogenous spread, and he has collected a short series of autopsy findings, discovered accidentally in the course of post-mortem work, which suggest the possibility of no less than three different periods of exogenous infection.

Terplan has also taken pains to define the terms which are in many publications used all too loosely. He would restrict re-infection to those cases in which all the anatomical evidence points to a new infection from without, but in the presence of a healing or actually healed older lesion, and he would further confine the term super-infection to instances where an additional infection from without can be proved in an individual who already has an active lesion. In his view re-infection should not be used for such things as tuberculous meningitis, miliary tuberculosis and tuberculous pneumonia where there is an extension of the lesions or disease from an existing complex. In other words, there should indeed be a definite free interval of considerable duration between the time of the first infection and the second manifestation of tuberculosis. All this work has led Terplan to the view that a better understanding of the pathogenesis of tuberculosis would be reached by the elimination of the terms childhood and adult types altogether. A lesion of primary type may occur in adults, and this is not necessarily the effect of re-infection.

The most difficult lesions of all to assess in the adult are the solitary foci. They are usually roughly spherical, of fairly uniform density and have sharply

defined borders (Pierson). Three types have been described, (1) the Assman early infiltration (Morlock), a caseous pneumonic infraclavicular lesion; (2) the circular foci of Fraenkel and others, a circumscribed lesion like that in a kidney or other metastatic extrapulmonary deposit of tuberculosis and not confined to the subapical region of the lung; (3) the pulmonary tuberculomata—solitary foci of tubercle without surrounding inflammation and probably the same structures as Fraenkel's circular foci. Numerous explanations of their origin have been given—viz., isolated metastatic deposits, blocked bronchi and unusual examples of primary foci in adults. If they are part of a primary complex, albeit a very unusual type, their importance in our discussion today is obvious.

Blood dissemination cannot be fitted into a time sequence of events. It is a sabotage phenomenon, a spanner thrown into the wheels of the machine at any phase, and we have no means of controlling it.

Conclusions must be tentative, but one thing seems clear: the terms endogenous and exogenous have served their purpose and should disappear. Meanwhile, the old order is changing. Not only is the incidence of the disease declining but the age at onset is moving from childhood to the adult years, and we are looking at a pathological picture which, during this transitional period, displays at least five types of lesions: (*a*) childhood type of primary focus which heals, (*b*) childhood type which goes on to cavitation, broncho-pneumonia and death, (*c*) childhood type which smoulders on until cavity formation in adult life, (*d*) the primary focus in an adult known to have been previously tuberculin negative—which is the type seen in the hospital nurse with post-primary clinical manifestation such as pleural effusion—and (*e*) healed childhood lesion with an adult re-infection of the primary type, in which the latter may heal too or pass on progressively to post-primary and bronchogenic tuberculosis.

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DETECTION OF TUBERCLE BACILLI BY THE FLUORESCENCE TECHNIQUE

By J. W. CLEGG and A. F. FOSTER-CARTER

From the Brompton Hospital

Since Hagemann's (1937) original account of the use of fluorescence microscopy for detecting tubercle bacilli a number of other arrangements of the apparatus have been described (Lind and Shaughnessy; 1942, Graham, 1942; and

Lempert, 1944, to mention only a few). All these have certain technical defects, chiefly lack of contrast and poor illumination. The apparatus described here is the outcome of our efforts to overcome these difficulties; for more than a year it has been used for all the routine examinations at the Brompton Hospital in preference to the Ziehl-Neelsen method. Results show that the method is at least as accurate as the other; while the ease with which bacilli can be seen at low magnifications makes it much quicker and far less tiring.

Principle

For those unfamiliar with the method a brief account of the principle of fluorescence microscopy will be useful. Tubercle bacilli in the microscopic preparation are stained with auramine, a yellow dye which fluoresces when exposed to ultra-violet light. Light from a source rich in ultra-violet is passed through a filter absorbing all except violet and ultra-violet rays (Fig. 1); these pass through the microscope and are themselves absorbed by a yellow filter in the eyepiece. No direct light from the lamp reaches the eye. But, in their passage through the microscope, the ultra-violet rays impinge on the preparation, causing the auramine-stained tubercle bacilli to fluoresce; this fluorescence is clearly visible through the yellow eyepiece filter, so that the bacilli appear brilliantly illuminated against a dark background.

Apparatus

Light Source.—This is the most important single item in the equipment. It must be small, even and highly concentrated and must be rich in ultra-violet radiation. We found that the B.T.H. Mazda mercury vapour electric discharge lamp (Box type, ME 250 w./50/5, shown in Fig. 2) fulfilled our requirements and was better than other sources of illumination that we tried, including the " Mercra " lamp (Lempert, 1944). It provides a small, concentrated mercury vapour arc, 5 mm. by 1·6 mm. in size, of high brilliance and even intensity, and it is very simple to manœuvre. The total consumption from the supply on A.C. is about 285 watts and the lamp may be operated from either A.C. or D.C. mains through an appropriate control box. Full details of this lamp are given by Bourne (1943).

Ultra-Violet Filter.—The most satisfactory filter that we have yet found consists of a glass cell, at least 1½ inches deep, filled with ammoniacal copper sulphate solution ($CuSO_4$, 5 gm.; NH_4OH, 30 c.c.; H_2O, 270 c.c.). A Roux bottle answers very well. This filter transmits freely wavelengths from 4,200Å to the ultra-violet region; absorption increases from 4,200 to 5,200 Å, above which point it absorbs very heavily.

A simple convex lens projects the image of the light source on to the microscope mirror. The lamp, ultra-violet filter and condensing lens are conveniently housed in a ventilated light metal casing to prevent the escape of stray light (Fig. 1).

Yellow Eyepiece Filter.—Ideally, this should absorb all the rays passed by the ultra-violet filter; we have obtained the best results so far using an Ilford " Delta " photographic filter (No. 109). This consists of thin dyed gelatin

cemented between slips of glass; a ½-inch diameter circular filter fits neatly into most microscope eyepieces. This filter transmits freely wave lengths from 5,200 Å upwards; absorption increases from 5,200 to 4,800 Å, and it absorbs blue, violet, and ultra-violet very heavily. It has one small disadvantage, slight general fluorescence of the dyed gelatin, but this is not sufficient to impair the results.

No other special apparatus is required. The rays which cause the fluorescence are those just at the end of the visible spectrum, rather than the extreme

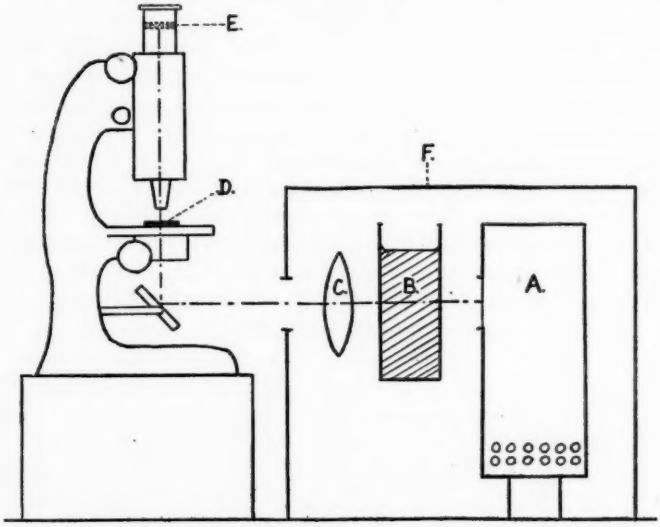

FIG. 1.

A=lamp; B=ultra-violet filter; C=condensing lens; D=stained preparation; E=yellow filter; F=casing of lamp unit.

ultra-violet (Graham, 1942). These rays pass through ordinary glass, so there is no need to use quartz lenses or an aluminium surfaced mirror.

So far it has been difficult to get filters for experiment, but it is hoped that both existing filters may be replaced in the future by others of dyed glass, matched to give more complete absorption. This would increase contrast between the fluorescing bacilli and the background.

Staining Technique

Sputum Smears.—(Lempert, 1944). Formulæ: *Stock 3 per cent. Phenol.*—Make from pure crystals dissolved in distilled water, and keep in a well-stoppered bottle.

Auramine-Phenol Solution.—Take 100 c.c. stock 3 per cent. phenol solution; warm to 40° C. (using an asbestos mat on a tripod); add 0·3 gm. of auramine (Gurr); shake vigorously for ten minutes. The turbid yellow solution is filtered and is then ready for use; it becomes clear on standing and will keep for three weeks in a well-stoppered dark bottle.

PLATE I.

FIG. 2.—MAZDA MERCURY VAPOUR LAMP.

FIG. 3.—PUS IN SMALL BRONCHIAL TUBE CONTAINING LARGE NUMBERS OF BACILLI. (Magnification × 1000.)

[*To face page* 100.

Acid-Alcohol Decoloriser.—0·5 c.c. conc. HCl; 0·5 gm. NaCl; 75 c.c. methylated spirit; 25 c.c. distilled water.

Counterstain.—0·1 per cent. potassium permanganate in distilled water.

Method: Stain with auramine-phenol solution for four minutes; wash well with tap water; decolorise for four minutes; wash well with tap water; counterstain for thirty seconds; wash with tap water; blot, and allow to dry.

Smears stained in this way and examined by fluorescence microscopy can be superstained by the Ziehl-Neelsen method as a check.

Method of Use

Switch on the lamp and allow at least six minutes for it to warm up. Then centre the lamp with the microscope; this is best done by holding a piece of thin white paper over the microscope and centring the image of the arc projected on to the paper. Insert the cell of ammoniacal copper sulphate solution between the lamp and the microscope, and place an auramine-stained smear of sputum known to be *strongly* positive on the stage. Insert the eyepiece containing the yellow filter and focus the smear with the $\frac{2}{3}$-inch objective. Illumination is faint, but, with care, the preparation may be focused without much difficulty; the background should appear very dark, but tinged with yellow. Manipulate the sub-stage condenser until a small area dotted with brilliant yellow points of light appears in the centre of the field; these are tubercle bacilli fluorescing in the beam of ultra-violet light, which is now correctly focused on the preparation. The final step is to insert the condensing lens between the lamp and the microscope; its position is then adjusted to enlarge the area of fluorescence as much as possible. The cover is placed over the lamp unit, and, if the components are not moved, the apparatus remains ready for use. If the microscope is removed, the position of its base should be marked so that it can be replaced in exactly the same place. It is then easy to readjust the mirror and sub-stage condenser, using the stained specimen of strongly positive sputum. This specimen, or a similar one from a culture, should be teeming with tubercle bacilli; if so, it will be an invaluable adjunct when setting up the microscope.

With a $\frac{2}{3}$-inch objective the bacilli appear as tiny yellow points of light clearly seen because of their brilliance. Using this objective large areas can be searched rapidly. Suspicious fluorescent points can be identified by substituting the $\frac{1}{6}$-inch objective. Even at this comparatively low magnification the shape of the bacilli is clearly seen, and an immersion lens need never be used—a great advantage over the Ziehl-Neelsen method. If an immersion objective is used, glycerin or oil of wintergreen should replace the customary cedar-wood oil, which fluoresces.

Fluorescence microscopy is particularly useful for detecting tubercle bacilli in paraffin sections of tissues, and it is far superior to the Ziehl-Neelsen technique for this purpose. The sections may be counterstained with methylene blue or with hæmatoxylin and eosin. The latter dyes themselves fluoresce slightly, so that the structure of the tissue can be seen faintly in relation to the brilliantly illuminated tubercle bacilli (Fig. 3).

Results

It is not universally accepted that the auramine method of staining is as specific for tubercle bacilli as the Ziehl-Neelsen method. To test this we first used the laborious method tried by Lempert, making duplicate slides of each specimen and staining one by each technique. Of some 300 specimens examined, not one was found to be negative by the auramine staining, yet positive by the Ziehl-Neelsen. On the other hand, several which were rapidly positive by the fluorescence technique proved very difficult to confirm by the Ziehl-Neelsen staining. It was then discovered that tubercle bacilli already stained by auramine could still be stained satisfactorily by Ziehl-Neelsen technique. After that, when bacilli were either very scanty or appeared atypical by the fluorescence method, their position was marked on the slide, which was then stained by the Ziehl-Neelsen technique. The bacilli always stained satisfactorily. When they were very scanty or atypical in shape the specimen was cultured to confirm their presence. Altogether some 900 specimens and 20 cultures were examined in this way. The results of this preliminary assay appeared to justify the introduction of the fluorescence technique as a routine measure.

The next step was to determine the reliability of the fluorescence method as a routine laboratory procedure. This was done by analysing the results obtained in a large series of specimens and comparing these with results obtained in other laboratories using the Ziehl-Neelsen technique on similar specimens. We have analysed the results in a consecutive series of sputa sufficiently large to yield 500 which were negative on direct examination or concentration. The specimens referred to in this analysis were all derived from patients in one of the following categories: the majority were from cases where the diagnosis was in doubt; others came from cases of pulmonary tuberculosis making good clinical progress with, or without, collapse therapy, and who were expected to become sputum negative; the remainder were from cases with radiological evidence of healed tuberculosis only. All cases of active tuberculosis were disregarded, as it was felt that such material was valueless for comparison. In addition to sputa, pleural fluids and gastric lavages from patients falling into these three categories were examined by the fluorescence method. The results are included in the analysis. Thus the material under review amounts to 748 specimens (Table 1).

TABLE 1.—SPECIMENS EXAMINED

Sputum	586
Pleural fluid	100
Gastric lavage	62
	748

Sputum Examinations.—In 586 consecutive specimens of sputum from these groups of patients, 78 were positive by the fluorescence method on direct examination; 8 more were positive on concentration. The 500 negative sputa were all cultured on Lowenstein's medium, yielding 56 more positive results. These findings are set out in Table 2.

TABLE 2.

Positive.	*Sputum.*	*Pleural Fluid.*	*Gastric Lavage.*
Direct examination	78	21	—
Concentration	8	—	4
Culture	56	23	10
Negative	444	56	48
Total	586	100	62

Table 3 summarises the clinical diagnosis in the 444 cases which were negative on culture. It will be seen that no less than 197 of them were found to be suffering from conditions other than tuberculosis. These included many cases of bronchiectasis, non-specific inflammatory conditions and new growths.

TABLE 3.—ANALYSIS OF CASES WITH T.B. NEGATIVE RESULTS MICROSCOPICALLY AND CULTURALLY

	Sputum.	*Pleural Fluid.*	*Gastric Lavage.*
Clinically tuberculous	247	50	42
Non-tuberculous	197	6	6
Total	444	56	48

Pleural Fluids.—During this period 100 pleural fluids were examined from similar sources. Twenty-one were positive on direct examination, and 23 more yielded cultures of *M. tuberculosis* (Table 2). This left a residuum of 56 cases in which it was not possible to demonstrate the tubercle bacillus; 50 of these were clinically tuberculous and 6 were proved to be non-tuberculous (Table 3).

Gastric Lavage.—During the same period 62 gastric lavages were done. Four were positive on direct examination by the fluorescence method and 10 more gave positive cultures (Table 2). In the 48 cases where tubercle bacilli were not demonstrated 42 were considered, on clinical grounds, to be tuberculous. The remaining 6 had other conditions (Table 3).

Discussion

It should be emphasised that the clinical state of patients from whom these specimens were obtained was such that in many a positive result was not anticipated because the disease was clinically arrested or healed. Yet of 742 specimens examined, 111 (14·9 per cent.) were found to be positive by the fluorescence method, and a further 89 (11·5 per cent.) yielded a positive culture. It was subsequently shown that 209 of these specimens were derived from patients who were proved to be suffering from conditions other than tuberculosis. Thus the number of specimens from patients suffering from clinical tuberculosis is reduced to 539. Of these specimens, 20·6 per cent. were positive by the fluorescence method, and a further 16·5 per cent. yielded positive cultures, giving the total for the combined methods of 37·1 per cent.

The chief difficulty in attempting a comparison between the published

results obtained in various laboratories using a variety of techniques lies in the uncertainty that the groups of specimens under review are strictly comparable. Clearly, in any series containing a high proportion of active cases of tuberculosis the percentage of positive results will be correspondingly high with any of the recognised methods of identification conscientiously carried out.

The most suitable series of cases comparable to our own is that of Webster (1941-1943). He examined 1,340 Army recruits who, as a result of mass radiography, were thought to be suffering from tuberculosis. He classified these cases, on clinical and radiological grounds, in the following groups: active tuberculosis 505, doubtful active tuberculosis 237, healed tuberculosis 374, doubtful tuberculosis 234. If the active cases are excluded from his series, as from our own, there remain 835 cases which appear strictly comparable with our own. The method employed by Webster was to examine the sputum from those recruits who could provide a satisfactory sample. This was examined by the Ziehl-Neelsen technique, and cultures of the concentrated specimen were made when the smear was negative. Recruits unable to provide a suitable specimen of sputum (a considerable proportion) all had a gastric lavage done after fasting overnight. This material was also examined by the Ziehl-Neelsen technique, and cultured if the direct examination was negative. Table 4 gives a comparison of the two series. The percentage of positive findings by the fluorescence method is thirteen times as large as by the Ziehl-Neelsen method. It follows that either there is a marked difference in the sensitivity of the two methods, or alternatively a marked difference in the clinical criteria adopted in the two series. While we admit that there may be some variation in these criteria, we find it inconceivable that this can account

TABLE 4

Total	*Positive by Microscopy.*			*Positive by Culture.*		*Combined Positive.*	
	Ziehl-Neelsen.	*Fluorescence.*	*Per Cent. Positive.*	*Total.*	*Per Cent.*	*Total.*	*Per Cent.*
835 Webster's series	9	Not used	1·1	67	8·5	76	9·2
748 Our series	Not used	111	14·9	89	11·5	200	26·8

for more than a small part of the difference. Consequently we feel that we can at least claim that the fluorescence method is more sensitive than the Ziehl-Neelsen method without making any extravagant claim as to precisely how much more sensitive it may be.

Summary

1. An apparatus is described in detail for the routine examination of pathological fluids for tubercle bacilli by the fluorescence method. It has proved entirely satisfactory.

2. Results are given of the examination of 748 consecutive specimens derived from patients suffering from either arrested or healed tuberculosis,

or from cases in which the diagnosis was doubtful; 111 of these specimens were positive by the fluorescence method, and an additional 89 specimens gave positive cultures.

3. These results are compared with a similar series published by Webster (1943).

4. We find the fluorescence method just as accurate, more sensitive, and more rapid than the Ziehl-Neelsen technique. We recommend the fluorescence technique to any laboratory where large numbers of examinations for tubercle bacilli are done.

We wish to thank Mr. P. W. Bliss and Mr. H. K. Bourne of the British Thomson-Houston Co., Ltd., for their co-operation and advice about the "Mazda" lamp. We also wish to thank Mr. W. Goodwin for his keen and accurate technical assistance throughout the investigation.

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REPORTS OF SOCIETIES

JOINT TUBERCULOSIS COUNCIL

The principal business at the Joint Tuberculosis Council Meeting on May 18 was the discussion of a report of an interview between representatives of the Ministry of Health and representatives of the Council on the position of the Tuberculosis Service under the National Health Bill.

According to a note of the interview made by J.T.C. representatives, the Tuberculosis Service, as it exists at present, will disappear. Tuberculosis Officers will become "Chest Physicians" dealing with all chest conditions. These chest physicians will be in charge of chest clinics in hospitals. They will have no responsibility over non-pulmonary tuberculosis, which will be dealt with by other departments of hospitals. Preventive work, together with home nursing and social service, will remain with the medical officers of health. The chest clinics, however, will come under the new regional hospital authorities. So far as is known, the only integration of these two arms of service will be achieved through conferences presided over by the principal regional medical officers. Whole-time tuberculosis nurses will be exceptional in future, as tuberculosis cases will be included in the proposed new general health visiting and nursing service of local authorities. Rehabilitation, in its clinical aspect, will be controlled regionally by the Ministry of Health, and in its employment aspect by the Ministry of Labour.

The Joint Tuberculosis Council regard the Minister's proposals as gravely inadequate and as constituting a danger to the public health. They view with alarm the separation of the social, environmental and epidemiological aspects of tuberculosis from the purely clinical aspect. They hold strongly to the view

that the family and not the patient should be the unit. They reject the Ministry's implied assumption that tuberculosis requires no differentiation from other diseases. No matter how the disease manifests itself in any individual, they say, he requires prolonged special supervision of his mode of life and of his environment. This is essential, not merely for his own safety, but for the safety of the community. This special supervision should be the responsibility of someone with special knowledge of the disease and of each individual case.

The Council record their emphatic opinion that no attempt should be made by the Government to break down the existing service until a scheme is produced which is at least as well integrated and as satisfactory as the best schemes of the present day. Certainly the existing service should not be altered until the incidence and mortality of tuberculosis have declined to a low level.

The Joint Tuberculosis Council assert that the best interests of the tuberculosis patient and of the community would be served if the existing service were transferred intact to the new hospital organisation and retained in that organisation as an entity.

The views of the Council are to be communicated to all Members of Parliament, all local authorities, the medical profession generally, and all persons or bodies specially interested in tuberculosis.

Some months ago the Minister of Health stated in the House of Commons that tuberculosis patients were entitled to supplementary ration allowances. The Joint Tuberculosis Council took up the statement, and after a protracted correspondence have received a statement to the effect that:

1. Tuberculous patients in institutions are entitled to normal civilian rations and points goods.
2. Tuberculosis institutions, along with other institutions, are entitled to priority supplies of goods such as dried eggs, jellies, etc.
3. Tuberculous patients are granted 2 pints of milk per day and 2 ozs. of cooking fat per week instead of the normal civilian allowances of these foods. In addition, if the institution concerned possesses a deep fat frier, a special allowance of 2 ozs. per head per week of frying fat can be obtained.

The Council feel that this announcement should receive publicity because the Minister's statement last November was open to misinterpretation.

IN MEMORIAM

GEORGE JESSEL, M.A., M.D., D.P.H.

MANY of our readers will have heard with surprise and regret of the unexpected death of George Jessel. He was one of a dwindling band of the old guard of tuberculosis officers who took office in 1913 and grew in stature with the years. Able and ambitious and a ready debater with a clear head, he did good work in the wide field of prevention and treatment of tuberculosis and had scope for his abilities in Lancashire and on many councils and committees. He combined first-rate clinical work with that degree of administrative ability which together make the outstanding tuberculosis officer.

In these days of excessive specialisation his varied and successful medical

training before he entered the tuberculosis service is not without interest. He graduated in 1906 from University College, Oxford, and qualified from the London Hospital the same year. Resident for a year at the London, where he had won the Anderson prize in clinical medicine, and also resident for a year at the Great Ormond Street Children's Hospital, he then spent two years in private practice. The D.P.H. at Manchester in 1913 under Delépine, where he was first man of the year, and the M.D. Oxon in 1917 completed a very sound training.

Tuberculosis work started in 1913 when Jessel was appointed a combined tuberculosis officer for a Lancashire county area and also for the county borough of Wigan. This, like other similar appointments, was an interesting experiment which failed because the tuberculosis officer was under two masters, competing for his services. In 1919 he became a whole-time officer solely under the Lancashire County Council as a consultant tuberculosis officer of one of the newly formed big areas containing a population of some 370,000. This area contained the Peel Hall Pulmonary Hospital, of which he was throughout the visiting medical superintendent. There he did excellent work, especially with artificial pneumothorax when this treatment was very little known and less used. Treatment, graduated work and hobby ocupations were organised to a high degree of efficiency. His own words give an insight to his character: " The tuberculosis officer who aims at realising the ideals of his office must undertake somewhat the rôle of schoolmaster and cleric as well as medical specialist."

The integration of hospital with clinic and domiciliary work carried out by a team, which has been the foundation of the Lancashire scheme, had its birth in Dr. Jessel's area, and his successful advocacy and carrying out of this union played a prominent part in its adoption for the whole administrative county.

Throughout his career he was actively connected with the N.W. Branch of the Society of Medical Officers of Health and the N.W. Tuberculosis Society, and was a past president of both these bodies. He did good work at the Joint Tuberculosis Council, for long was its treasurer, and at the time of his death vice-chairman. His wide knowledge of tuberculosis and clear vision of its public health and social implications were always at the service and to the benefit of the many committees of the Council on which he served.

His main hobby was photography, hence his enthusiasm for X-ray work carried out at a high level, making him a valued member of the Minister of Health's committee which prepared the way for mass miniature radiography.

To his widow, son, and two daughters we extend our sympathy in their bereavement.

G. L. C.

REVIEWS OF BOOKS

The Problem of Lupus Vulgaris. By ROBERT AITKEN, M.D., F.R.C.P.E., F.R.S.E., Lecturer in Diseases of the Skin, Edinburgh University; Physician to the Skin Department, the Royal Infirmary of Edinburgh. Edinburgh: E. and S. Livingstone, Ltd. Pp. 69. 15s.

This small book is, as a book, a joy to handle. Printed on fine paper, the type is clear and pleasing to the eye; the quality of the illustrations, half of them in natural colour, taken from the author's own collection of photographs,

is admirable. The first four chapters deal with the clinical features and the accepted and proven methods of treatment. Most space is devoted to ultra-violet irradiation, locally by the Finsen-Lomholt lamp combined with general light baths by the carbon arc lamp. The author has great experience of these methods, and the results, as the photographs show, are excellent. Dr. Aitken amply proves the first of his two chief points, that lupus is a curable disease. The second point, the existence of the *problem* of lupus, forms the forcible last chapter, which should be read with benefit, and perhaps shame, by all practitioners, public health authorities, even by dermatologists. The problem is one of education, finance and organisation, and while the author points out that a comprehensive hospital service might prove of great value, he stresses that so far " the salaried service has proved every bit as unsatisfactory as the private practice."

It is unfortunate that the book was written before the general appreciation in this country of the value of calciferol in treatment of lupus, which seems likely to alter, if not almost to abolish, the problem of lupus. It is not, however, a " cure-all," and there will still be many cases requiring the older treatment so well set out in this book.

A. H. B.

Notable Names in Medicine and Surgery. Second Edition. By HAMILTON BAILEY and W. J. BISHOP. H. K. Lewis, London. Price 15s.

It is a tribute to the attractions of this little book that it has already found its way into a second edition. The authors promise, too, that it shall soon be accompanied by a second volume—" More Notable Names "—to fill in some of the gaps inevitably left in the first. There are no changes in the text of this edition, but some ingenious rearrangement in the printing has allowed for more than thirty new or different illustrations. Among the most notable of these are a coloured picture of tubercle bacilli in sputum, several clear anatomical diagrams, and a drawing, reproduced from Esmarch's textbook, of a delightfully nonchalant amputation. The new volume may be awaited with pleasure.

J. S.

N.A.P.T. Handbook of Tuberculosis Activities. Twelfth Edition, 1946. Edited by HARLEY WILLIAMS, M.D. Published by The National Association for the Prevention of Tuberculosis, London, W.C.1. Price 7s. 6d.

In a neat form and dress this useful handbook of tuberculosis schemes and activities makes a welcome reappearance under the auspices of the N.A.P.T. It still serves, as formerly, the need for a well-documented directory; and to its former lists of local authority schemes, sanatoria and hospitals for the treatment of tuberculosis are added on this occasion details of mass radiography units, centres for thoracic surgery, and particulars of the tuberculosis facilities in the Dominions and Colonies, as well as a miscellaneous amount of information for those dealing with tuberculosis.

The preparation of this new edition must clearly have involved a great deal of revision and correction. Perhaps in future editions the amount of information might be more carefully sifted and apportioned between the large and the small institution or scheme; and the list of contents could be improved by page references, if not supplemented by a suitable index. But these are minor criticisms, and the book remains the one available directory of its kind.

C. H.